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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/370,453 | 08/09/1999 | DAN W. DENNEY JR. | GENITOPE-038 | 8128 |

23535 7590 02/13/2007

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| EXAMINER | |
|---|---|
| CANELLA, KAREN A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1643 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 02/13/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/370,453 | DENNEY | |
| | Examiner | Art Unit | |
| | Karen A. Canella | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) 25-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 25-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 25-29 are pending and under consideration.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The instant claims require a cell expressing a multivalent composition for active idiotype therapy, wherein said it a T lymphoid parent cell line wherein at least one expression vector has been introduced, wherein said multivalent composition expressed by said cell include Vh and Vl regions from malignant B cells isolated from a patient having quasi-clonal B cell lymphoma. The post filing art teaches the administration of idiotype protein conjugated to KLH, wherein the idiotype protein is recombinantly expressed from lymphoma cells taken from patients and thus represents the spectrum of B cell idiotypes of the malignant cells from the individual patient (Timmerman et al, Blood, Nov 16, 2005, Vol. 106, pp 685A-686A; Leonard et al, Blood, Nov 16, 2003, Vol. 102, page 105A; and Leonard et al, Blood, Nov 16, 2002, vol. 100, abstract no. 4792). The instant composition differs from the composition of the post filing art in that the transformed T cell is the agent for active idiotype immunotherapy. Thus, when given the broadest reasonable interpretation, administration of the cell of the instant claims would be

expected to evoke an immune response against a spectrum of quasi-clonal malignant B cells within an individual patient. This is not enabled by the specification for the following reasons. The art teaches that malignant B cells fail to evoke an anti-tumor response because said cells do not express the co-stimulatory molecules of CD40L, B7.1, ICAM-1 and LFA-3, and thus fail to activate T cells in vivo (Briones et al, Blood, Nov 16, 2001, Vol. 98, page 608A). The art teaches that non-activated T cells cannot respond optimally without this second signal provided by the co-stimulatory molecules, and if said T cells recognize their respective antigens without the co-stimulatory signal the T cell becomes inactivated producing a state of tolerance (Roitt et al, Immunology (text), 1998, page 142, first column, first paragraph). In the event that the transformed T cell of the invention produced enough of the idiotype protein in the context of MHC it fails to possess the co-stimulatory molecules that would result in T cell activation of resting T cells upon recognition of the transformed T lymphoid cell of the instant invention because T cells do not activate other T cells Thus, although the T cells of the invention would have the co-stimulatory molecules of CD28, CD40L, LFA-1 and CD2 as part of the T cell receptor, these co-stimulatory molecules do not interact with other T cells to provide an activating signal (Roitt et al, ibid, page 143, figure 11.8).. Further, transformation of the T lymphoid cells with the expression vector encoding the idiotypic proteins is not expected to alter the affinity of the T cell receptor which would function to bind to the MHC of the malignant B cell. There is no objective evidence that MHC expression of a T cell can substitute for a TCR in the recognition of surface antibodies on B cells and result in an activated T cell. The specification fails to address this lack of stimulatory ability and fails to teach how a T cell expressing antigens from malignant B cells can exert an immune stimulation when administered to a patient having the same malignant B cells. Given the lack of teachings regarding how to overcome the immune tolerance associated with a cell which does not express co-stimulatory molecules necessary for the activation of T cells, one of skill in the art would be subject to undue experimentation in order to use the claimed T cells for active idiotype immunotherapy.

All previous rejections and objections as set forth or maintained in the previous Office action are withdrawn in light of applicants arguments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
2/5/2007